

The reaction is a stereoselective reaction as one diastereomer is primarily formed. That one diastereomer is primarily formed is an important issue.

First, this achieved effect is a surprising one, as there is no such teaching or suggestion in the prior art, that by using an ortho-lithiating group for the introduction of a secondary phosphino group, one of two possible diastereomers is primarily formed providing an enantiomeric excess of one of the possible diastereomers.

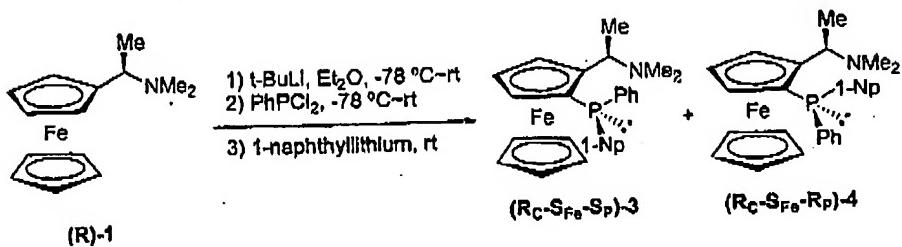
Second, that one of the two possible diastereomers is primarily formed is also a big advantage over the prior art as it is the aim of the invention to provide ligands having chiral phosphino groups for use in asymmetric catalytic reactions, e.g. see the first sentence of page 1 of the description stating:

"This invention relates to a novel process for the production of asymmetric transformation catalysts, in particular to such a process for the production of phosphine and arsine ligands having a chiral centre at phosphorus, or arsenic as the case may be." (Emphasis added)

The "production of asymmetric transformation catalysts" signifies working with **enantiopure** catalysts, i.e. working with only one of at least two possible diastereomers.

Thus, if a racemate of diastereomers is obtained, the diastereomers have to be separated prior to their use as a ligand in an asymmetric catalytic reaction. Therefore, it is a huge advantage if one of the diastereomers is already primarily (or even solely) formed.

The Experimental section in the specification is useful to illustrate this effect. Here is an extract of Example 3:



"The ratio of $(\text{R}_C, \text{S}_{\text{Fe}}, \text{S}_P)$ -3 to $(\text{R}_{\text{Cl}}, \text{S}_{\text{Fa}}, \text{R}_P)$ -4 is about 5:1. As $(\text{R}_C, \text{S}_{\text{Fe}}, \text{R}_P)$ -4 is insoluble in cold hexane and $(\text{R}_C, \text{S}_{\text{Fe}}, \text{S}_P)$ -3 is very soluble in cold hexane, the two isomers can be easily separated by crystallization from hexane." (Emphasis added)

Examples 6 and 7 are useful to illustrate that even **pure diastereomers** can be obtained.

In summary, the instant invention provides a diastereoselective reaction as one diastereomer is primarily formed.

There is no teaching or suggestion in this direction to be found in Hayashi et al. (or any other prior art).

The disclosure of the instant invention uses the wording "chiral" with the meaning of enantiopure throughout the description and experimental section. This is apparent from the first page of the description stating that:

"The invention also relates to **chiral catalysts** produced by the process of the invention, and to the use of such catalysts in **asymmetric** transformation reactions.

Ferrocene as a backbone for diphosphine ligands was introduced by Kumada and Hayashi based on the pioneering work of Ugi related to the synthesis of **enantiopure** substituted metallocenes¹." (Emphasis added) (See last sentence in paragraph [0001] and paragraph [0002] of Applicants' published application US 2008/0281106 A1).

As the skilled artisan knows that only an enantiopure catalyst is usable in asymmetric catalytic reactions, it will be apparent to him/her that the description is concerned with the production and possible use of enantiopure ligands.

The Examiner's argument is that:

1. The prior art contains all claimed features, however, not in one single document.

2. The skilled artisan would be able to combine these features (from different documents).
3. The skilled artisan would expect the results as being obvious.

However, Applicants respectfully submit that:

1. The skilled artisan would not combine the features in the references.
2. These features would not necessarily fulfill the same function if combined.
3. The results were not foreseeable.

Applicants will initially demonstrate that the results provided by the instantly claimed process were not foreseeable.

Hayashi et al. disclose the stereoselective introduction of a phosphine group in ortho-position, however, the phosphine group is **not a (phosphor)-chiral group**. Further, as already discussed this reference does not teach or suggest that an ortho-lithiating group might have a diastereoselective effect.

Nettekoven et al. do not disclose or suggest the use of an ortho-directing group to build up a phosphor-chiral group. The disclosed method for introducing p-chiral groups is using a totally different approach.

Berlin et al. is cited by the Examiner for disclosing a Grignard reaction for introducing different groups R on a phosphor atom. However, Berlin et al. clearly teach away from a Grignard reaction, as explained below.

Berlin et al. are concerned with unsymmetrical phosphine oxides of the type $\text{Ar}_2\text{P}(\text{O})\text{R}'$. Two synthetic routes are disclosed, one is a Grignard reaction on which the Examiner relies. However, with regard to the Grignard reaction Berlin states on page 78 at the beginning of the second paragraph that:

"condensation of diphenylphosphinic chloride and the Grignard reagent 3 gave 1 in yields which averaged 15%."

Further the article states at the top of page 79 that:

"... this second method .. is to be recommended in preference to the Grignard experiment."

See also "Preparation of 1 via a Grignard reaction" (last paragraph on page 80 up to and including the first two paragraphs on page 81), concluding that:

"the Grignard reaction was Inferior to that from the rearrangement process".

As the paper clearly states that the **Grignard reaction is not recommended, it would not motivate the art-skilled to use this method.**

Furthermore, phosphine (V) oxides of the type $\text{Ar}_2\text{P}(\text{O})\text{R}'$ are not chiral.

In summary:

Berlin et al. are not concerned with chiral phosphines,

Berlin et al. teach away from using the Grignard reaction,

Nettekoven et al. do not disclose or suggest the use an ortho-directing group to build up a phosphor-chiral group,

Hayashi et al. do not teach or suggest chiral phosphino groups, and

Hayashi et al. do not teach or suggest a stereoselective effect by using an ortho-lithiating group.

Consequently, an attempt to combine the teachings of the three cited documents would not lead to the conclusion that the results of the instantly claimed invention were foreseeable. Furthermore, despite the fact that the Examiner has repeated his line of argument as to why the prior art documents may be combined in order to arrive at the instant invention, Applicants submit that **the references cannot be combined in a meaningful way.**

For these reasons, Applicants take the position that the rejection of the claims under 35 U.S.C. §103(a) should be withdrawn.

The Examiner has also repeated the provisional rejection of claims 38-44 for obviousness-type double patenting as being unpatentable over claims 44 and 54-60 of Serial No. 10/586,287. On page 3 of the Office Action, the Examiner states that he cannot hold the rejection in abeyance because the policy of the PTO is to apply all applicable rejections as early as possible to facilitate compact prosecution.

As noted in MPEP 804, section A, where the Examiner becomes aware of two co-pending applications that were filed by the same inventive entity, the courts have sanctioned the practice of making applicants **aware of the potential double patenting problem** if one of the applications became a patent by permitting the examiner to make a "**provisional**" rejection on the ground of double patenting; and moreover, the "**provisional**" double patenting rejection should continue to be made by the Examiner in each application as long as there are conflicting

claims in more than one application unless that “provisional” double patenting rejection is the only rejection remaining in at least one of the applications. The Examiner has not indicated in an Office Action that the “provisional” double patenting rejection is the only remaining rejection in at least one of the applications. Therefore, the Examiner should continue to make the “provisional” double patenting rejection in subsequent actions.

Further, since the Examiner has made Applicants aware of the “provisional” rejection, no further action is required at this time. “Once the provisional rejection has been made, there is nothing the examiner and the applicant must do until the other application issues.” See *In re Mott*, CCPA 1976, 539 F.2d 1291, 190 USPQ (BNA) 536. “There is no question of course, that a double patenting rejection would be proper if one of appellant’s applications issues. The effect of our reversal is merely to maintain co-pendency of these claims.” The Court further noted that where the PTO refuses to permit further prosecution without performance by the appellant, such as by cancelling, arguing distinctions, or amending the claims, the rejection, in legal effect, is final and improper. Therefore, no action can be taken after a “provisional” rejection has been made unless one of the applications has issued. Since neither applications has issued in the present case, the Examiner cannot properly require Applicants to distinguish or amend the claims or file a Terminal Disclaimer.

Moreover, since amendments may be made to either application during their pendency, the Examiner must wait until one application issues before requiring the filing of a terminal disclaimer. “If a ‘provisional’ non-statutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later filed application is rejectable on other grounds, the examiner should withdraw the rejection and permit the earlier-filed application to issue as a patent without a Terminal Disclaimer.” MPEP 804. Clearly, the MPEP does not require the filing of a Terminal Disclaimer unless one of the applications has issued.

Therefore, in view of the foregoing remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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